CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2

TI Method for producing L-amino acids by fermentation using DNA gyrase **inhibitor** resistant bacterial strains

AN 2001:207978 CAPLUS

DN 134:221524

TI Method for producing L-amino acids by fermentation using DNA gyrase **inhibitor** resistant bacterial strains

IN Kino, Kuniki; Abe, Tetsuya

PA Kyowa Hakko Kogyo Co., Ltd., Japan

SO Eur. Pat. Appl., 6 pp.
CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1085086	A2	20010321	EP 2000-120125	20000919
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2001157596	A2	20010612	JP 2000-280075	20000914
	US 6344347	B1	20020205	US 2000-663795	20000918
PRAI	JP 1999-265107	A	19990920		

TI Method for producing L-amino acids by fermentation using DNA gyrase **inhibitor** resistant bacterial strains

AB The present invention provides an industrially efficient method for producing an L-**amino acid** useful as medicament, chem. agent, food material and feed additive, and the method comprising culturing in a medium a microorganism having an ability to produce the L-**amino acid** and having **resistance** to a DNA gyrase **inhibitor** or a microorganism having an ability to produce the L-**amino acid** and having both **resistance** to a DNA gyrase **inhibitor** and **resistance** to an aminoquinoline deriv., producing and accumulating the L-**amino acid** therein and recovering the L-**amino acid** therefrom. In particular, the invention provides L-histidine prodn. mutant Echerichia coli strains having both **resistance** to a DNA gyrase **inhibitor** and **resistance** to an aminoquinoline deriv. Two Echerichia coli strains H-9342 and H-9343 were obtained by a mutation treatment with N-methyl-N'-nitro-N-nitrosoguanidine of a L-histidine-producing mutant strain H-9340 having **resistance** to 1,2,4-triazole alanine, which was derived from methionine-requiring **Escherichia** coli ATCC 21318.

ST **amino acid** prodn DNA gyrase **inhibitor** resistant bacteria fermn; histidine prodn DNA gyrase **inhibitor** resistant bacteria fermn

IT **Arthrobacter**
Bacilli
Corynebacterium
Escherichia
Microbacterium
Microorganism
Serratia
(DNA gyrase **inhibitor** resistant mutant of; method for producing L-amino acids by fermn. using DNA gyrase **inhibitor** resistant bacterial strains)

IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(DNA gyrases, **inhibitor**, **resistance** to; method for producing L-amino acids by fermn. using DNA gyrase **inhibitor** resistant bacterial strains)

IT Fermentation

PARENT

Ref V

TI REQUIREMENT OF DNA GYRASE FOR THE INITIATION OF CHROMOSOME REPLICATION IN **ESCHERICHIA**-COLI K-12.

AN 1980:209873 BIOSIS
DN BA70:2369

TI REQUIREMENT OF DNA GYRASE FOR THE INITIATION OF CHROMOSOME REPLICATION IN **ESCHERICHIA**-COLI K-12.

AU FILUTOWICZ M
CS INST. BIOCHEM. BIOPHYS., POL. ACAD. SCI., UL. RAKOWIECKA 36, PL-02-532 WARSZAWA, POL.

SO MOL GEN GENET, (1980) 177 (2), 301-310.
CODEN: MGGEAE. ISSN: 0026-8925.
FS BA; OLD
LA English

TI REQUIREMENT OF DNA GYRASE FOR THE INITIATION OF CHROMOSOME REPLICATION IN **ESCHERICHIA**-COLI K-12.

AB Strains carrying mutations in the dnaA gene are unusually sensitive to COU [**coumermycin**], NAL [**nalidixic** acid] or NOV [**novobiocin**], which are known to inhibit DNA gyrase activities. The delay in the initiation of chromosome replication afte COU treatment was observed in cells with chromosomes synchronized by **amino acid** starvation or by temperature shift-up (dnaA46). The unusual sensitivity of growth to COU of the initiation mutant runs parallel to a higher sensitivity to the drug of the initiation of chromosome replication. The double mutant, dnaA46 cou-110, was isolated and mutation cou-110 conferring **resistance** of growth, initiation and elongation of chromosome replication to COU was mapped in the gene coding for the subunit of DNA gyrase. The reduced frequency of appearance of the mutants resistant to COU, NAL or NOV in the initiation mutant suggests that some mutations in genes coding for DNA gyrase subunits cannot coexist with the dnaA46 mutation. The possible mechanisms of the requirement of DNA gyrase for dnaA-dependent initiation of E. coli chromosome are discussed.

IT Miscellaneous Descriptors
COUMERMYCIN NALIDIXIC-ACID **NOVOBIOCIN** ENZYME **INHIBITOR**-DRUG METABOLIC-DRUG

RN 303-81-1 (**NOVOBIOCIN**)
389-08-2 (**NALIDIXIC**-ACID)
78040-85-4 (**COUMERMYCIN**)

AB Strains carrying mutations in the dnaA gene are unusually sensitive to COU [**coumermycin**], NAL [**nalidixic** acid] or NOV [**novobiocin**], which are known to inhibit DNA gyrase activities. The delay in the initiation of chromosome replication afte COU treatment was observed in cells with chromosomes synchronized by **amino acid** starvation or by temperature shift-up (dnaA46). The unusual sensitivity of growth to COU of the initiation mutant runs parallel to a higher sensitivity to the drug of the initiation of chromosome replication. The double mutant, dnaA46 cou-110, was isolated and mutation cou-110 conferring **resistance** of growth, initiation and elongation of chromosome replication to COU was mapped in the gene coding for the subunit of DNA gyrase. The reduced frequency of appearance of the mutants resistant to COU, NAL or NOV in the initiation mutant suggests that some mutations in genes coding for DNA gyrase subunits cannot coexist with the dnaA46 mutation. The possible mechanisms of the requirement of DNA gyrase for dnaA-dependent initiation of E. coli chromosome are discussed.

TI Nucleotide sequence, mutational analysis, transcriptional start site, and product analysis of nov, the gene which affects **Escherichia** coli K-12 **resistance** to the gyrase **inhibitor novobiocin**

Reference U

AN 1995:467923 CAPLUS

DN 123:104086

TI Nucleotide sequence, mutational analysis, transcriptional start site, and product analysis of nov, the gene which affects **Escherichia** coli K-12 **resistance** to the gyrase **inhibitor novobiocin**

AU Ivanisevic, Radmila; Milic, Mirjana; Ajdic, Dragana; Rakonjac, Jasna; Savic, Dragutin J.

CS Inst. Mol. Genetics Genetic Engineering, Belgrade, Yugoslavia

SO J. Bacteriol. (1995), 177(7), 1766-71
CODEN: JOBAAY; ISSN: 0021-9193

DT Journal

LA English

TI Nucleotide sequence, mutational analysis, transcriptional start site, and product analysis of nov, the gene which affects **Escherichia** coli K-12 **resistance** to the gyrase **inhibitor novobiocin**

AB In a previous study, we demonstrated the existence of a gene locus, nov, which affects **resistance** of **Escherichia** coli K-12 to the gyrase **inhibitor novobiocin** and, to a lesser degree, coumeromycin (j. Rakonjac, M. Milic, D. Adjic, D. Santos, R. Ivanisevic, and D. J. Savic, Mol. Microbiol. 6:1547-1543, 1992). In the present study, sequencing of the nov gene locus revealed one open reading frame that encodes a protein of 54,574 Da, a value found to be in correspondence with the size of the Nov protein identified in an in vitro translation system. We also located 5' end of the nov transcript 8 bp downstream from a classical sigma70 promoter. Transcription of the gene is in the counterclockwise direction on the E. coli chromosome. Transposon mutagenesis of nov followed by complementation analyses and replacement of chromosomal alleles with mutated nov confirmed our previous assumption that the nov gene exists in two allelic forms and that the Novr gene is an active allele while the Nos gene is an inactive form. After comparing nucleotide sequences flanking the nov gene with existing data, we conclude that the gene order in this region of the E. coli K-12 map is att.phi.80-open reading frame of unknown function-kch (potassium channel protein)-nov-opp. Finally, the possible identity of the nov gene with cls, the gene that codes for cardiolipin synthase, is also discussed.

ST nov gene **Escherichia** sequence mapping

IT **Escherichia** coli
(nucleotide sequence and product anal. of the nov gene that affects **Escherichia** coli K-12 **resistance** to gyrase **inhibitor novobiocin**)

IT Genetic mapping
(of nov gene and flanking markers; nucleotide sequence and product anal. of the nov gene that affects **Escherichia** coli K-12 **resistance** to gyrase **inhibitor novobiocin**)

IT Deoxyribonucleic acid sequences
(of nov gene of **Escherichia** coli; nucleotide sequence and product anal. of the nov gene that affects **Escherichia** coli K-12 **resistance** to gyrase **inhibitor novobiocin**)

IT Protein sequences
(of nov gene product of **Escherichia** coli; nucleotide sequence and product anal. of the nov gene that affects **Escherichia** coli K-12 **resistance** to gyrase **inhibitor novobiocin**)

IT Enzymes
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(DNA-supercoiling, nucleotide sequence and product anal. of the nov gene that affects **Escherichia** coli K-12 **resistance** to gyrase **inhibitor novobiocin**)

IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cls, possible identity of nov gene and; nucleotide sequence and product anal. of the nov gene that affects **Escherichia** coli K-12 **resistance** to gyrase **inhibitor novobiocin**)

IT Gene, microbial
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nov, nucleotide sequence and product anal. of the nov gene that affects **Escherichia** coli K-12 **resistance** to gyrase **inhibitor novobiocin**)

IT Genetic element

TI Superhelical **Escherichia** coli DNA: Relaxation by **coumermycin**.
AN 78317726 EMBASE
DN 1978317726
TI Superhelical **Escherichia** coli DNA: Relaxation by **coumermycin**.
AU Drlica K.; Snyder M.
CS Dept. Biol., Univ. Rochester, N.Y. 14627, United States
SO Journal of Molecular Biology, (1978) 120/2 (145-154).
CODEN: JMOBAK
CY United Kingdom
DT Journal
FS 037 Drug Literature Index
004 Microbiology
029 Clinical Biochemistry
030 Pharmacology
LA English
TI Superhelical **Escherichia** coli DNA: Relaxation by **coumermycin**.
AB Folded chromosomes isolated from E.coli strains after treatment with **coumermycin** A1 in vivo, an **inhibitor** of DNA gyrase were found to have reduced DNA superhelical densities. This loss of DNA supercoiling paralleled inhibition of DNA synthesis. **Coumermycin** also produced a loss of supercoiling in non-replicating chromosomes that had been synchronized by **amino acid** starvation. The drug had no effect on supercoiling in chromosomes isolated from a mutant bacterial strain from which Gellert et al. found **coumermycin** -resistant gyrase activity. Thus, the correlation between **coumermycin** inhibition of cell growth, DNA synthesis, and in vitro gyrase activity now extends to the loss of chromosomal DNA supercoiling. It appears that DNA gyrase may be responsible for the maintenance of negative supercoiling in the E.coli chromosome. Moreover, the chromosomal DNA remained intact after drug treatments, indicating that loss of supercoiling arises from the action of a DNA-relaxing activity.
CT Medical Descriptors:
*2 aminomethylhydroxybiphenyl derivative
*cell growth
*chromosome
*coumamycin a
*density gradient
*dna supercoiling
*dna synthesis
***drug resistance**
*enzyme inhibition
***escherichia coli**
*thymidine h 3
in vitro study
animal experiment
methodology
heredity
therapy
controlled study
Drug Descriptors:
*coumamycin a1
*dna
*dna topoisomerase (atp hydrolysing)
*ethidium bromide
radioisotope
AB Folded chromosomes isolated from E.coli strains after treatment with **coumermycin** A1 in vivo, an **inhibitor** of DNA gyrase were found to have reduced DNA superhelical densities. This loss of DNA supercoiling paralleled inhibition of DNA synthesis. **Coumermycin** also produced a loss of supercoiling in non-replicating chromosomes that had been synchronized by **amino acid** starvation. The drug had no effect on supercoiling in chromosomes isolated from a mutant bacterial strain from which Gellert et al. found **coumermycin** -resistant gyrase activity. Thus, the correlation between

Ref 28

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TI **Escherichia** coli cells resistant to the DNA gyrase **inhibitor**, ciprofloxacin, overproduce a 60 kD protein homologous to GroEL.

AN 90121912 EMBASE

DN 1990121912

TI **Escherichia** coli cells resistant to the DNA gyrase **inhibitor**, ciprofloxacin, overproduce a 60 kD protein homologous to GroEL.

AU Hallett P.; Mehlert A.; Maxwell A.

CS Department of Biochemistry, University of Leicester,Leicester LE1 7RH, United Kingdom

SO Molecular Microbiology, (1990) 4/3 (345-353).
ISSN: 0950-382X CODEN: MOMIEE

CY United Kingdom

DT Journal; Article

FS 004 Microbiology
037 Drug Literature Index

LA English

SL English

TI **Escherichia** coli cells resistant to the DNA gyrase **inhibitor**, ciprofloxacin, overproduce a 60 kD protein homologous to GroEL.

AB Using a variety of mutagenic methods, we have generated a series of ciprofloxacin-resistant mutants derived from **Escherichia** coli strains which overproduce the DNA gyrase A protein. Many of these mutants are found to overexpress a 60 kD protein which is shown to be highly homologous in terms of N-terminal **amino acid** sequence to the E. coli heat-shock protein, GroEL. Other evidence confirms that the 60 kD protein is unrelated to DNA gyrase and is similar, but not identical, to GroEL.

CT Medical Descriptors:
***antibiotic resistance**
***escherichia coli**
immunoblotting
mutagenesis
plasmid
nonhuman
article
priority journal
Drug Descriptors:
dna topoisomerase
*ciprofloxacin
nalidixic acid
norfloxacin
oxolinic acid

RN (dna topoisomerase) 80449-01-0; (ciprofloxacin) 85721-33-1; (**nalidixic** acid) 389-08-2; (norfloxacin) 70458-96-7; (**oxolinic** acid) 14698-29-4

AB Using a variety of mutagenic methods, we have generated a series of ciprofloxacin-resistant mutants derived from **Escherichia** coli strains which overproduce the DNA gyrase A protein. Many of these mutants are found to overexpress a 60 kD protein which is shown to be highly homologous in terms of N-terminal **amino acid** sequence to the E. coli heat-shock protein, GroEL. Other evidence confirms that the 60 kD protein is unrelated to DNA gyrase and is similar, but not identical, to GroEL.

RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(method for producing L-amino acids by fermn. using DNA gyrase **inhibitor** resistant bacterial strains)

IT **Escherichia** coli
(strain H-9342 or H-9343; method for producing L-amino acids by fermn. using DNA gyrase **inhibitor** resistant bacterial strains)

IT 71-00-1P, Histidine, preparation
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(method for producing L-amino acids by fermn. using DNA gyrase **inhibitor** resistant bacterial strains)

IT 54-05-7, Chloroquine 86-42-0, Amodiaquine 86-78-2, Pentaquine 90-34-6, Primaquine 303-81-1, **Novobiocin** 389-08-2, **Nalidixic** acid 4434-05-3 14698-29-4, **Oxolinic** acid 31135-62-3, Aminoquinoline
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**resistance** to; method for producing L-amino acids by fermn. using DNA gyrase **inhibitor** resistant bacterial strains)

AB The present invention provides an industrially efficient method for producing an L-**amino acid** useful as medicament, chem. agent, food material and feed additive, and the method comprising culturing in a medium a microorganism having an ability to produce the L-**amino acid** and having **resistance** to a DNA gyrase **inhibitor** or a microorganism having an ability to produce the L-**amino acid** and having both **resistance** to a DNA gyrase **inhibitor** and **resistance** to an aminoquinoline deriv., producing and accumulating the L-**amino acid** therein and recovering the L-**amino acid** therefrom. In particular, the invention provides L-histidine prodn. mutant Echerichia coli strains having both **resistance** to a DNA gyrase **inhibitor** and **resistance** to an aminoquinoline deriv. Two Echerichia coli strains H-9342 and H-9343 were obtained by a mutation treatment with N-methyl-N'-nitro-N-nitrosoguanidine of a L-histidine-producing mutant strain H-9340 having **resistance** to 1,2,4-triazole alanine, which was derived from methionine-requiring **Escherichia** coli ATCC 21318.